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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/619,493	07/19/2000	Norman Nashed	SCH-1686-C1	1582

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EXAMINER	
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ART UNIT	PAPER NUMBER
1616	18

DATE MAILED: 10/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/619,493	Applicant(s) NASHED, NORMAN	
	Examiner Sabiha Qazi	Art Unit 1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *15 July 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *17* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

FINAL ACTION

Acknowledgement is made of the response filed in paper no. 17, dated 7/15/03. Claims 1-25 are pending and rejected. Amendments are entered.No claim is allowed.This application is a division of 09/331,397, filed on 6/21/1999 (now abandoned), which is a 371 of PCT/DE97/03032, filed on 12/22/1997. Claims 1-23 are drawn to the method of treating premenstrual dysphoric disorder (PMDD) by administering gestagen alone or in combination of estrogens. Since the specification does not have support for such broad claims and this field a minor change in concentration even a different method of administeration make thongs different. One would not expect the results unless undue experimentation.

The first paragraph of 35 U.S.C. 112 states, "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same...".

The courts have interpreted this to mean that the specification must enable one skilled in the art to make and use the invention without undue experimentation.

The courts have further interpreted undue experimentation as requiring "ingenuity beyond that to be expected of one of ordinary skill in the art" (Fields v. Conover, 170 USPQ 276 (CCPA 1971)) or requiring an extended period of

experimentation in the absence of sufficient direction or guidance (In re Colianni, 195 USPQ 150 (CCPA 1977)). Additionally, the courts have determined that "... where a statement is, on its face, contrary to generally accepted scientific principles", a rejection for failure to teach how to make and/or use is proper (In re Marzocchi, 169 USPQ 367 (CCPA 1971).

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Colianni, 195 USPQ 150, 153 (CCPA 1977), have been clarified by the Board of Patent Appeals and Interferences in Ex parte Forman, 230 USPQ 546 (BPAI 1986), and are summarized in In re Wands (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed Cir. 1988). These factors were discussed in detail in our last office action.

Applicant should limit their claims to a genus, which finds full support in the specification and should amend the claims to clearly show the criticality of their invention. This means what is unexpected which was not taught nor suggested by the prior art of record.

Claim Rejections - 35 USC § 112

Claims 1-25 rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Following reasons apply.

1. In evaluating the enablement question, several factors are to be considered. *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

1) The nature of the invention: Instant claims are drawn to the method of treating premenstrual dysphoric disorder (PMDD) by administering gestagen alone or in combination of estrogens such as ethinylestradiol, estratriene triol, dialkyl derivatives of estradiol, dienogest, drospirenone, cyrosterone acetate, estrogen, estradiol valerate, estradiol ester, gestagen and others.

2) The state of the prior art: Prior art of record teaches method of treatment of Premenstrual syndrome (PMS) by gestagen and also in combination with estrogen. PMDD is now identified as a distinct clinical entity with characteristic symptoms of irritability, anger, internal tension, dysphoria and mood lability. PMDD is the more severe form of premenstrual symptamology, whereas premenstrual syndrome (PMS) is milder and more prevalent.

3) The predictability in the art: There is a general lack of predictability in the pharmaceutical art. *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970). Therefore, predicting which gestagen or its combination with any estrogen will be useful in the treatment of PMDD is impossible.

4) The presence or absence of working examples: On page 2 of the specification 1-11, PMDD symptoms are listed. The specification asserts that PMDD can be effectively treated by gestagens and also in combination of estrogesn. On page 9, last para, after the treatment over 4-6 cycles with 3 mg of drospirenone and 30ug of ethinylestradiol, "a significant improvement relative to at least one of the symptoms (as numbered 1-4) that occurred before the beginning of the treatment, but not only the 11th symptom, is observed". There is no data what specific symptoms were treated.

Applicants "significant improvement" does not explain what symptoms were improved? How many women were studied in the experiment and whether other estrogen-gestagen combination or gestagen would work. Some symptoms of Premenstrual syndrome (PMS) and PMDD are similar and overlap. There is no test data, which would assist the skilled artisan in practicing the claimed invention. The skilled artisan, seeking lead compounds for pharmaceutical discovery and treatment of PMDD, would be at a loss as to where to begin such discovery in the absence of such data.

5) The breadth of the claims: The claims are drawn not only to the method of treatment of PMDD by broad class of gestagen which is itself broad, but also to combination of estrogens which encompasses hundreds of different species.

One may look to, Dennertein et al. (British Medical Journal, Vol. 200, pages 1617-1621), which discloses a trial and effects of progesterone and premenstrual symptoms, see Table I on page 1619, Table III on page 1620. Table I on page 1619 shows a list of premenstrual complaints reported by number of women. It should be noted that irritability is at the top of complaint list. Irritability is also a PMDD symptom and various symptoms of PMS and

PMDD overlap. The data as shown in Tables II and III clearly shows significance of progesterone treatment. See also "discussion" on page 1620, where progesterone treatment is favored. Specification fails to specifically indicate the novelty of the treatment.

Another reference of interest may be for example Andersch et al. (J. of Psychosomatic Res.) where administration of progesterone to 15 women premenstrual symptoms after and before the treatment are listed in Table 1 on page 491. The reference also discloses that a closer look at some subgroups would be women with swelling but no mental symptoms, with mental but no swelling symptoms, and those unfortunate women with severe symptoms of both kinds. The beneficial effects of prostaglandin inhibitors on some premenstrual symptoms are of great interest but its possible tetragenic effects hamper its use in the luteal phase. Furthermore, the reference concludes that there is no single medication that has proved effective against all symptoms that can be met with in the premenstrual period.

See also Johan Gullberg, where mood changes and menstrual symptoms with different Gestagen/Estrogen combinations are disclosed, see especially Table 2.1 on page 12-13 and figure 8.2 on page 43.

6) The quantity of experimentation needed: Since the nature of the method is so unpredictable, as can be seen by the prior art cited above and since the claims are drawn to a broad range of pharmaceuticals for treatment of PMDD and since there is a lack of guidance present in the specification, the skilled artisan would have to undertake undue experimentation to practice the claimed invention commensurate with the scope of the claims.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

1. Claims 1-25 rejected under 35 U.S.C. 103(a) as being unpatentable over Dennertein et al. (British Medical Journal, Vol. 200, pages 1617-1621), and Johan Gullberg. These two references cited teach the method, which embraces instantly claimed invention. See the entire documents especially in Dennertein, which discloses a trial and effects of progesterone and premenstrual symptoms see Table I on page 1619 and Table III on page 1620. Table I on page 1619 shows a list of premenstrual complaints reported by number of women. It should be noted that irritability is at the top of complaint

list. Irritability is also a PMDD symptom and various symptoms of PMS and PMDD overlap.

The data as shown in Tables II and III clearly shows significance of progesterone treatment. See also "discussion" on page 1620, where progesterone treatment is favored.See Table 2.1 on page 12-13 and figure 8.2 on page 43 in Gullberg reference which teaches the Mood Changes and Menstrual Symptoms with different Gestagen/Estrogen combinations"

Instant claims differ from the reference in claiming broader scope than the prior art. For example treatment of PMDD by gestagen and combination with estrogen, natural or synthetic wherein specific estrogen and estrogen are claimed for the treatment.

It would have been obvious to one skilled in the art to prepare compositions for the treatment of premenstrual symptoms as the above-cited references teach the treatment with gestagen and with combination of gestagen and estrogen. The studies show positive effects of the treatment. Therefore, the disclosure of the cited references obviously would lead a person skilled in the art to use the conventional known gestagens or in combination with estrogen.

Example shown in the specification does not specifically shows any unexpected results, which were not taught by the prior art. Even though PMS and PM DD are distinct however, PMDD is considered a severe form of PMS. Since the method for treating is used to treat PMS, applicants must distinctly show their superiority of the invention.

Claims 1-23 rejected under 35 U.S.C. 103(a) as being unpatentable over Harvard Rev. Psychiatr. Vol. 2, No. 5, (1995), pages 233-245. The reference

teaches treatment of PMDD by progesterone or oestrogen which embraces Applicant's claimed invention. See the entire document especially page 234, right column and 235-236.

Clinical trials controlled studies are shown to have positive effects on symptoms such as irritation, anxiety, depression etc. In addition to effect of progesterone, the reference also discloses the positive effects of oestrogen, for PMDD treatment. see page 235-236.

The studies showed that subcutaneous or transdermally administered oestradiol improves a number of PMDD-related symptoms.

It would have been obvious to one skilled in the art at the time of invention to use the gestagens or oestrogen for the treatment of PMDD as taught by the prior art. In view of the teachings of the prior art of record cited above, a person skilled in the art would also consider administering a combination of the individual substances i.e. gestagen and oestrogen for treatment of PMDD for the reasons cited above.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Telephone Inquiry Contacts

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sabiha Qazi whose telephone number is 703-305-3910. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page can be reached on 703-308-2927. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

S. Qazi

SABIHA QAZI, PH.D
PRIMARY EXAMINER